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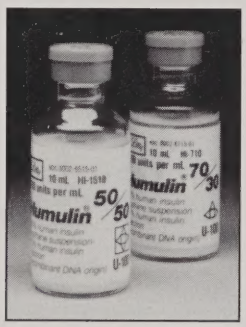

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THE
Hampden Hippocrat
MARCH—APRIL 1993

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The official bulletin for The Hampden District of the Massachusetts Medical Society. Founded in 1942 by Edward P. Bagg, Jr., M.D. and William A. R. Chapin, M.D.

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HAMPDEN DISTRICT MEDICAL SOCIETY 1992-1993 SEASON

ANNUAL MEETING

PLACE: **CARRIAGE HOUSE**
Old Storrowton Tavern
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SOCIAL HOUR: 7:00 p.m.

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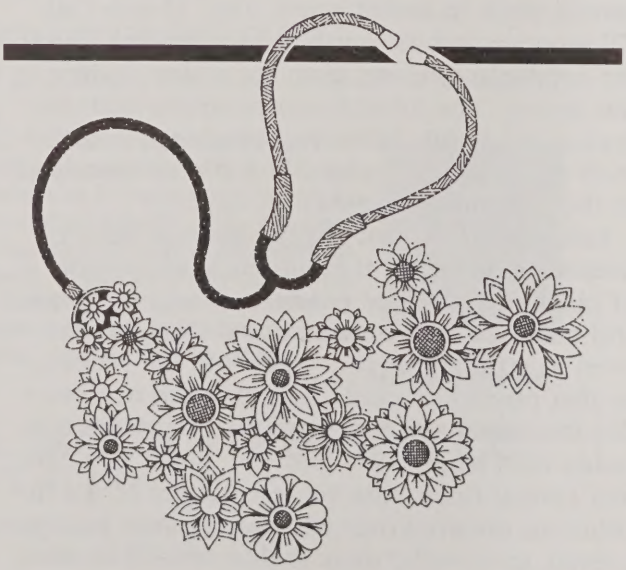
From the Editors

Transplantation—the goal of replacing damaged organs with intact ones from other humans or even animals—has been one of the major driving forces of medicine for the past thirty years. Our understanding of the immunologic system is a consequence of this. The paradigm of transplantation has resulted in marked refinements in our ethical understanding. Organ preservation is continually improving. Perhaps the political position that health care was a "right" began when dialysis and kidney transplantation became available to all citizens through Medicare.

There may, of course, be a downside. We are already seeing third-world transplant centers where organs of impoverished persons are purchased. Tissue from fetal brain is being transplanted into patients with Parkinson's disease. Will we soon have a new industry that pays for fetal parts? When we break through the species barrier and begin using baboon organs, it is likely that the cost of rendering the graft and host capable of living comfortably together will dwarf previous medical expenditures, and yet open up vast new possibilities for transplantation, since the ethical implications of using human parts would no longer exist, and since there would be no obligation to leave the donor intact.

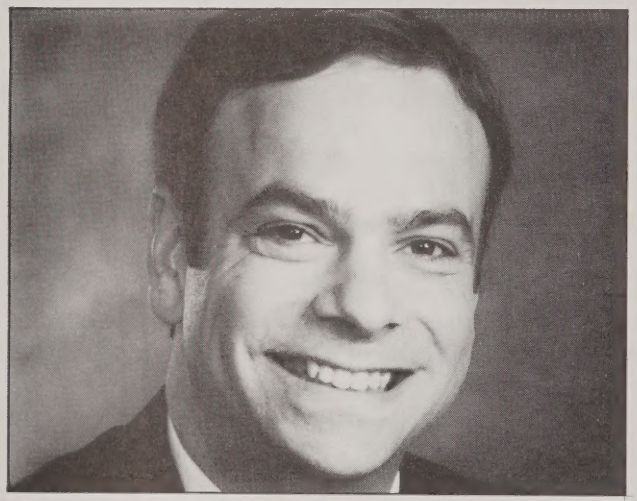
In the present issue, three articles are presented from the transplant program at Baystate Medical Center giving an overview of current issues in this field. ■

Brigid Glackin, M.D.
Donald J. Higby, M.D.
Co-editors



New Growth

As winter winds down and spring approaches, people naturally anticipate new growth. We expect sprouts to appear where seed was planted.



Robert V. Chircop, M.D., President

Hampden District Medical Society has planted several seeds in recent times. The "House Calls" TV program and the Anti-Smoking Poster Contest are familiar to all, and both are reality again this spring. The Educational programs with the Springfield Public School system are still in the early developmental stage. These were discussed in the previous President's Message.

Last year, Hampden District Medical Society undertook to lessen the burden to physicians, of obtaining privilege renewals at area hospitals and managed care organizations. Our goal has been to standardize and streamline the process, so that physicians could assemble the necessary documentation simultaneously for all such facilities, rather than singly, over and over again. We have met several times with representatives of the institutions involved over the course of the year. As a result, most will change their renewal processes this June to coincide with the physician's medical license renewal, which as you know, occurs on the physician's birthday, every other year. Needless to say, the changeover process will necessitate a shortened renewal cycle the first time around, but ultimately we'll all be a little less "hassled" as a result. We will continue to work with the few "hold out" institutions to gain their cooperation, pointing out the advantages to their personnel and Department Chairs. A letter from HDMS will accompany the renewal packets to help explain the shortened renewal cycle.

The newest development on the Public Health front is the formation by the Springfield Public Health Department, of a Community Neighborhood Health Center Task Force. HDMS is a member of this task force, and will give its assistance and insight as Dr. Deloris Williams, Commissioner, and the Task Force require. The Task Force is developing a master plan to address the Public Health needs of the city. Enhancements at the two existing Neighborhood Health Centers are planned, and a Federal grant application will be submitted by June '93 seeking funding for a new Neighborhood Health Center. Additional centers will be sought in years ahead as underserved neighborhoods are delineated and organized.

The Springfield Neonatal and Infant Mortality Study is still in the process of refining its data acquisition instruments. HDMS remains ready to assist the study with implementation of its recommendations, but that will await completion and reporting of their findings.

While our new initiatives appear in various early stages of formation, and will probably take some additional time and effort to take shape, the important observation to make now is that we are at least meeting the community in which we all work and live, and have become involved in addressing its collective needs and shaping its future. HDMS looks forward to pitching in. ■

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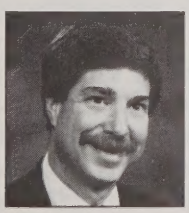

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Renal Transplantation—Progress And Prospects

Michael J. Germain, M.D., is a member of the Renal Division at Baystate Medical Center and Medical Director of the Renal Transplant Program.

Since the turn of the century, the technical aspects surrounding renal transplantation had been worked out in animals. As early as 1902, the kidney of a dog was transplanted to its neck vessels with urine flow. These experiments demonstrate the technical feasibility of auto-transplantation. Renal allografting (transplantation across individuals in a species) remained unsuccessful due to the immunologic barrier for the next 50 years.

"The program at Baystate...individualizes immunosuppression based on the patient's risk"

Interest was renewed in renal transplantation in the early 1950's due to advances in scientific knowledge concerning immunologic mechanisms involved in rejection of allografts. Renal allograft survival was still not possible because of the lack of availability of immunosuppressive agents. Of historical interest is the fact that one of the earliest successfully completed kidney transplant operations done in America was at the Springfield Hospital in 1951 by Dr. Scola. The patient died six weeks later with rejection of the kidney. Long-term chronic dialysis was not available at this time. It was not until 1954 when a kidney donated by an identical twin to his brother at Boston's Peter Bent Brigham Hospital was long-term success achieved in renal transplantation.

Renal transplantation with allografts was not successful long-term until 1961 when the drug azothiaprine, became approved for human use. The use of prednisone with azothiaprine became the standard regimen with successful long-term graft survival of 60%-70% at one year. Because of the lack of availability of chronic dialysis in the early days, heavy doses of immunosuppression were given repeatedly to reverse rejection that was refractory. This resulted in the patient's survival that was not much better than graft survival. In the early 1970's with the ready availability of chronic dialysis to all patients, less immunosuppression could be used and patient survival climbed to more than 90% where it has remained.

Combining anti-lymphocyte antibody preparation such as ALG (anti-lymphocyte globulin) and ATG (anti-thymocyte globulin) together with azothiaprine prednisone resulted in excellent graft survival in selected transplant programs in the early 1980's with graft survival at one year in the 80% range. It was not until commercial availability of cyclosporine in the mid 1980's that uniformly excellent graft survival was obtained in transplant centers throughout the country. Currently, 80% one-year graft survival is the norm across the country, while many centers, including our own, have a graft survival in the greater than 90% range. When cyclosporine and prednisone are combined with induction (anti-lymphocyte preparations including the newer monoclonal preparations, such as OKT3), greater than 90% graft survival is achievable. this potent type of immunosuppression, however, can result in serious immunocompromise and infections, CMV infection being the most important to recognize. The recent availability of gancyclovir has resulted in decreased morbidity and mortality from CMV, pneumonia, hepatitis and other complications.

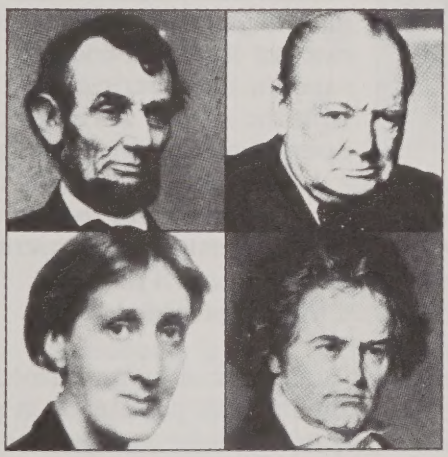
The renal transplant program at Baystate Medical Center has sought a different approach to immunosuppression. We attempt to individualize immunosuppression based on the patient's immunologic risk. We know, for instance,

that patients with repeat transplants, high levels of circulating cytotoxic antibodies and poor initial transplant function are more likely to have early rejection, and statistically worse graft survival. Those patients receive induction therapy with OKT3 while lower risk patients receiving just dual therapy with cyclosporine and prednisone. We have demonstrated with this protocol we can achieve equivalent graft survival in the high and low risk patient groups. We also feel that by minimizing immunosuppression in those patients who are low immune reactors, we avoid serious immunocompromised infections.

A number of new immunosuppressive agents are currently being studied and have the potential for significant improvement in graft survival, decreased rejection, and avoidance of the significance of neuro- nephro- and hepatic toxicity associated with cyclosporine. FK506 has been used clinically for approximately two years at the University of Pittsburgh in renal and hepatic transplants. Excellent graft survival in excess of 90% with very low incidence of rejection was seen. It does, however, have some nephrotoxicity similar to cyclosporine. Mizoribine and RS61443 are inhibitors of purine synthesis similar of azothiaprine but with much more potent immunosuppressive action without bone marrow suppression. Rapamycin and 15-deoxyspergualin are two new potent immunosuppressive agents that are synergistic with cyclosporine, and it is hoped low doses of these agents used together with low dose cyclosporine will result in an excellent graft survival with diminished toxicity from either agent. Finally, Brequinar, a drug that inhibits cell proliferation by blocking pyrimidine biosynthesis, may help induce a condition of graft tolerance and prevent chronic rejection which is currently the leading cause of long-term graft loss.

Two active areas of research in transplantation focus on the attempt to induce long-term immune tolerance and xenograft transplantation (the use of animal kidneys for human transplantation). The hope is that some of these newer immunosuppressive agents that are being developed may help to induce long-term tolerance in combination with other techniques to allow us to cross the xenograft barrier.

Currently, the most important issue in transplantation today is the availability of cadaver organs and how they are allocated. This is discussed in one of the companion articles in this issue. ■



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Pancreas And Pancreatic Islet Transplantation

Robert Madden, M.D., who contributed the following, is a transplant surgeon on the staff of Baystate Medical Center.

Pancreas transplantation was first performed in humans at the University of Minnesota in 1966. Because of low patient and graft survival rates with these early procedures, few pancreas transplants were attempted during the subsequent ten to fifteen years. In the early 1980's, however, the introduction of new immunosuppressive agents such as cyclosporine A and antilymphocyte globulins improved the results of organ transplantation and resulted in a renewed interest in pancreas transplantation as a cure for insulin dependent diabetes mellitus (IDDM).

Is the increased risk worth the possible benefit of being insulin free and perhaps avoiding the secondary complications of diabetes?

Over the past ten years, the number of pancreas transplants performed and the success rates have both increased. According to the Pancreas Transplant Registry (for cases in the United States reported to the United Network for Organ Sharing), approximately 1600 pancreas transplants were performed between October 1987 and December 1991. When performed concomitantly with a kidney transplant, patient survival in 1991 was 90% and pancreas graft survival was 76% at one year. Importantly, graft survival of the kidney in recipients of simultaneous pancreas/kidney (SPK) transplants was 84% at one year, which does not differ significantly from that of patients only receiving a kidney transplant (80%—one year kidney survival). In other words, by simultaneously transplanting a pancreas with a kidney, the chances for the patient to have a successfully functioning kidney are not reduced.

Since the first procedure, the technique of SPK transplantation has evolved through multiple phases. Today the operation has become relatively standardized in the United States. A single midline incision is used so that both organs can be transplanted through the same incision. The kidney is transplanted in a standard fashion with the renal artery and vein being anastomosed to the recipient external iliac artery and vein, respectively. The ureter is then anastomosed to the bladder using an antireflux technique. The pancreas is transplanted into the contralateral side of the pelvis. It is revascularized by anastomosing the donor portal vein to the external iliac vein and the superior mesenteric artery, with the splenic artery, to the external iliac artery. A short segment of donor duodenum is left attached to the pancreas and is anastomosed to the recipient urinary bladder for drainage of exocrine secretions from the transplanted pancreas. The native pancreas of the recipient is left undisturbed.

Pancreas transplantation can be performed alone in non-uremic diabetic patients or in patients who already have a functioning renal transplant, but is most commonly performed simultaneously with a kidney transplant. The pancreas graft survival rates with SPK transplants are significantly better than those of pancreas transplants performed alone because rejection episodes are more readily diagnosed. There is no accurate test to diagnose rejection of a pancreas graft (the onset of hyperglycemia usually indicates near-complete destruction of the transplanted beta cell mass) and the kidney is therefore used as a marker of rejection. When the creatinine increases and a renal biopsy

is consistent with rejection, the patient receives anti-rejection therapy. Most studies have shown that when the kidney and the pancreas are from the same cadaver donor, they most often reject simultaneously.

With regard to morbidity, the risks of SPK transplantation are greater than those of renal transplantation. The SPK operation is at least twice as long as a kidney transplant and requires more anastomoses. The dosages of immunosuppressants are often higher for recipients of SPK transplants which results in an increased incidence of postoperative infectious complications. These patients are also more prone to dehydration and metabolic acidosis as a consequence of the exocrine secretions from the transplanted pancreas being drained into the bladder.

To balance the risks, the beneficial effects of pancreas transplantation on the metabolic and secondary complications of diabetes should also be discussed. It is well established that successful pancreas transplantation results in normalization of both glycosolated hemoglobin levels and in recipient responses to glucose tolerance tests. There is, however, peripheral hyperinsulinemia because the insulin secreted by the transplanted pancreas is released into the peripheral circulation (recipient iliac vein). The insulin, therefore, does not undergo the first pass effect of the liver that occurs in non-diabetic individuals in whom insulin is released into the portal circulation. Although no adverse consequences have been observed, the long-term effect of these increased insulin levels remains unknown.

Studies of the secondary complications of diabetes in patients with pancreas transplants have yielded intriguing data. Evaluating mesangial volume and glomerular basement membrane thickness in diabetic patients who previously underwent renal transplantation, Bilious et al concluded that successful pancreas transplantation was associated with significantly less severe diabetic glomerulopathy in the transplanted kidneys. Kennedy et all compared a control group of diabetics to patients with a pancreas transplant and concluded that progression of diabetic neuropathy could be halted by successful pancreas transplantation. Ramsay et al, however, found that the progression diabetic retinopathy was not significantly reversed or prevented in diabetic patients with a functioning pancreas transplant at a mean follow up of 24 months. Overall, these early results are promising,

continued on next page

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Pancreas And Pancreatic

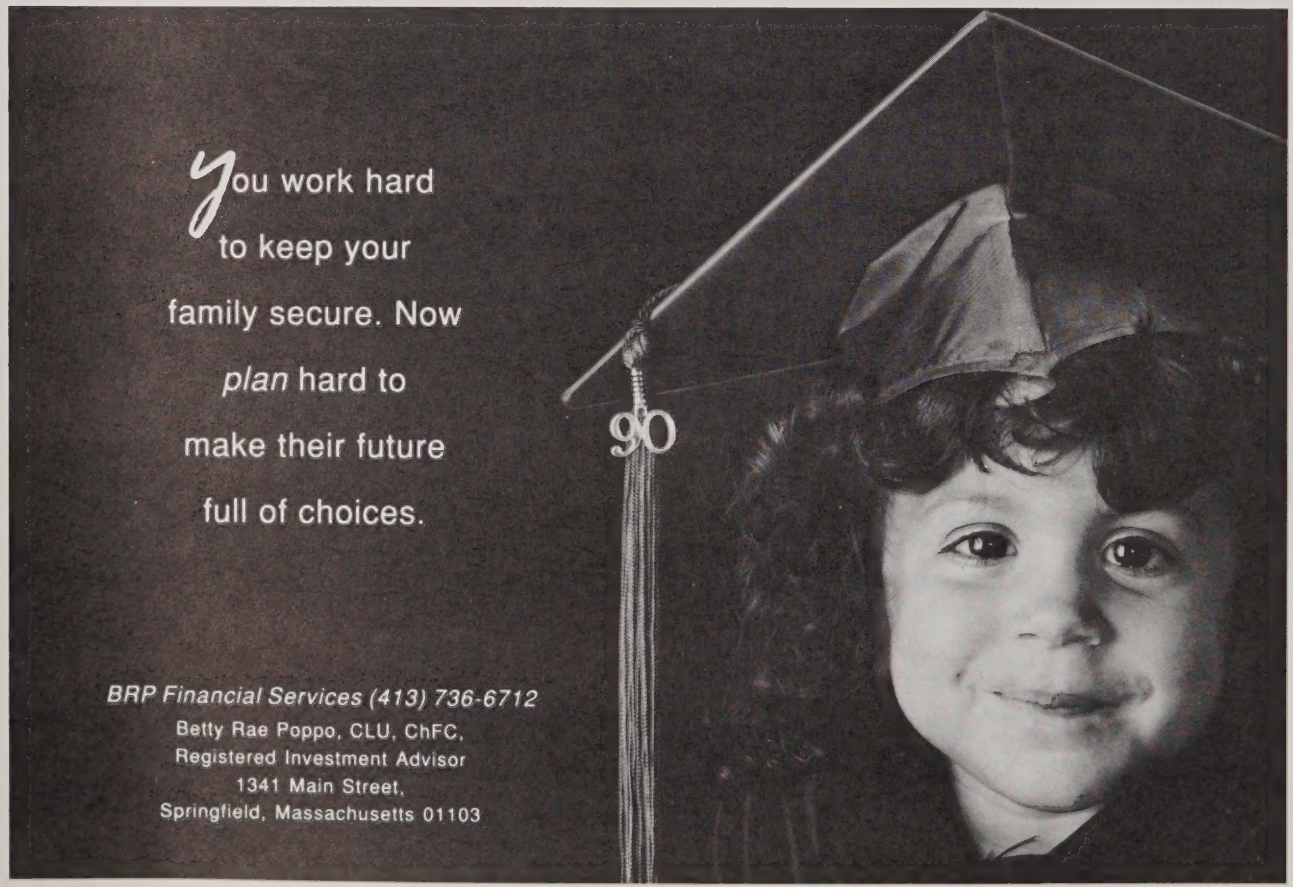
Continued from previous page

but the follow up is short. And as to whether these changes will produce a significant clinical impact on the secondary complications of patients undergoing pancreas transplantation remains unknown.

As an alternative to whole organ pancreas transplantation, some investigators are isolating pancreatic islets and transplanting them into diabetic recipients. Islets can be transplanted using a variety of techniques such as injection into the protal vein, encasement in prosthetic material and intraperitoneal placement, or placement under the capsule of the kidney or the liver. Despite success in multiple animal models attempts, to produce long-term euglycemia and insulin independence in diabetic patients have not yet been successful. The concept remains very appealing because islets can be rendered less immunogenic through pretransplant manipulation, and therefore, could theoretically be transplanted without using any postoperative immunosuppression. A substantial amount of research is being focused on the problems of islet transplantation, and with luck, this modality as a treatment for IDDM will become a reality.

At Baystate Medical Center (BMC), kidney and combined pancreas/kidney transplantaton are offered as treatment options for diabetic patients with end stage renal disease. To be considered for a SPK transplant, the paitent must have insulin *dependent* diabetes mellitus, end stage renal disease and must not have any contraindications for pancreas transplantation. Currently, the contraindications include significant, uncorrectable cardiac disease, active infection, malignancy, severe peripheral vascular disease, age greater than 50 years, tobacco/alcohol/drug abuse, and/or a history of noncompliance with medical therapy. Pancreas transplants alone and in patients with a functioning kidney transplant are not being performed at BMC.

As with all surgical prodcedures, the benefits of the operation must be weighed against the inherent risks. With regard to SPK transplantation, each patient must decide whether the increased risk of the procedure, as compared to renal transplantation is worth the benefits of being insulin free, and of possibly preventing the ravages of the secondary complications of diabetes. ■



Hampden Committee Activities

Dr. David Chadbourne, our secretary, reviews recent activities of HDMS committees.

The Public Health Committee's media campaign has gotten under way. The first in a series of articles was written on the topic of drinking responsibly. The article was published by the Springfield Union News and promoted by several area radio stations.

A House Calls Program on Smoking Cessation will coincide with our Third Annual Poster Contest. It will be held on Sunday, April 25, 1993.

The Credentialing Implementation Committee met in January. Almost every hospital and managed care plan has joined the program. It was decided that the hospitals would mail the reappointment forms on the physician's birthday when he/she gets his/her license renewal. The committee is set to meet again in May to finalize plans.

The Medico-Legal Committee met in January. Dr. Mark Mullan is the new Co-Chairman replacing Dr. Francis Murray. Attorney John Bagley remains as the Chair for the lawyers. The idea of a Charity Golf Tournament to be held in July was discussed. Everyone seemed agreeable to plans for a full day of golf, dinner and a raffle. Members of the Committee have developed a new form for requesting medical records and have reworked the Hampden County Medico-Legal Code. Final drafts will be approved at the next meeting in April. Also, a program to mediate problems in the medical and legal professions is being discussed, using three teams consisting of a doctor and a lawyer.

The Health Care Task Force is still working on setting up a communication program for bringing health information to students in the Springfield School System. Members of the committee are also working with the Springfield Health Department's new Community Health Center Task Force. The Health Department has applied for a grant to establish a new health center in the South End of Springfield.

Joseph T. Painter, M.D., President-Elect of the American Medical Association, was our featured speaker at the January 26th District Meeting, held at the Sheraton Springfield Monarch Place. The members in attendance enjoyed his speech as well as an excellent dinner. ■

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Update On Organ Donation

Marie Burns, R.N., CPTC, is the Donation Coordinator, New England Organ Bank. George S. Lipkowitz, M.D., is Director, Transplantation Services, Baystate Medical Center. They contributed the following.

There is a growing need for donated organs and tissues for transplantation. The United Network for Organ Sharing (UNOS) which is the federally designated Organ Procurement and Transplantation Network, reports that as of January 13, 1993 there were 29,585 registrations on the national patient waiting list. In New England, there are more than 1,300 candidates waiting. Sadly, about one-quarter of those patients waiting for organ transplants will die, as the result of a shortage of donated organs and tissues. There were only 13,766 organs available for transplantation in 1991. With continued advancements in preservation technology, improved surgical techniques, and immunosuppressive drug therapy to prevent rejection, success rates of transplantation continue to rise. The organ shortage is the single most limiting factor in transplantation today.

"One quarter will die as a result of a shortage of donated organs"

There is even a greater number of patients awaiting tissue transplantation. Examples are bone, skin, saphenous vein, heart valves and corneas. The availability of tissues for transplant is far greater than that of organs because tissue recovery can be done up to 12 hours after asystole and does not require the donor to have intact cardiovascular function. The New England Organ Bank, the organ procurement organization (OPO) covering most of New England, does "bank" tissue to be distributed to recipients in need.

The donation process consists of eight basic components; donor identification, referral, evaluation, consent, management recovery of organs, allocation, and follow-up. Each step in the process has gone through continued examination and revision in an effort to streamline and improve the donation process. The hospital's expert resource in the donation process is the OPO (New England Organ Bank).

There are several causes for the shortage of cadaveric organs in this country. The consent rate and factors that influence donor families has been closely examined. The current system of organ procurement being "expressed donation" is based on altruism. The Uniform Anatomical Gift Act of 1968 adopted in all 50 states was the first legislation to standardize the donation process. The most significant point was the establishment of the universal donor card. This allowed an individual to make the decision regarding organ and tissue donation prior to his death. Even though properly signing a donor card is a legally binding document to facilitate the donation process after your death, consent is almost always obtained from the legal next of kin to avoid potential legal liability. A Gallup survey undertaken for the partnership for Organ Donation in 1991 revealed that 84% of Americans approve of the donation of organs for transplantation. In fact, 73% indicated they would likely want their own organs donated upon death. Although 70% of those surveyed indicated they would be willing to discuss their feelings with their family, only 46% reported having done so. Less than half of those surveyed (42%) reported knowing that the next of kin must generally give permission for the organs to be donated, and 85% believed a potential donor must carry a signed donor card. This study along with many others send the theme that even though many individuals would desire to donate they do not sign a donor card or discuss their decision with their

family. Unfortunately, the majority of potential donors are younger people who have had a sudden and tragic death that leaves the family devastated and confused. Making any decisions at this time is difficult and not knowing the wishes of the deceased only complicates the decision making process. Many factors influence the consent process besides the absence of a signed donor card. The "required request" laws were passed to ensure all hospitals develop written protocols for identifying potential organ donors. This legislation is adopted in Massachusetts along with 43 other states and still has not resulted in an increase in organ donation.

The concept of "brain death" is the final step for families in coming to terms with donation. Frequently the family will continue to ask questions concerning this diagnosis and need repeated reassurance as to the concept of death begins to beome more of a reality to them. Once the family has acknowledged the death then the option to donate organs can be addressed. An early referral to the OPO will allow a trained donation coordinator to be immediately available to talk with the donor family. A study done by the Kentucky Organ Donor Affiliates from 1989 to 1990, revealed that if the discussion about brain death was separated from any discussion about the option to donate, then the consent rate improved dramatically.

The donor family needs to know that regardless of what organs or tissues are donated, the outward appearance of the individual is unchanged and an open casket is still an option. Disfigurement is the number one fear of the public. The donor family is reassured that all costs incurred after the time of death associated with the donation process are paid entirely by the OPO. If the donor family has religious concerns, it is advisable for them to consult with a clergy person of their own faith. All major Eastern and Western religions recognize donations as the highest form of selflessness and charity to your fellow man. The identity of the donor ramains confidential as does the recipients but the donor family is sent a letter of appreciation by the OPO with some information about the recipients. During the consent process these are a few of the issues addressed with the donor family.

What has emerged are several ideas to help improve the consent rate. Fininancial incentives

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Update On Organ Donation

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to donations and presumed consent are two approaches that have received a lot of attention and debate. The system of "presumed consent" would not require the consent of the donor family and would allow the routine organ procurement of suitable donors unless the donor has expressed his dissent prior to his death. The advantages to this system are thought by making organ donation a routine procedure would eliminate the decision of consent for donor families and they would simply be asked whether the individual had ever opposed or expressed his dissent to donation. It would also allow for recovery of organs if an exhausted search for the legal next of kin proved hopeless. The main objection to this system is the question of whether the potential donor had a lack of understanding of the option to "opt out" of donation and a valid system to record that opposition. It is thought that the widespread vigorous education required to allow for the public to understand their rights under presumed consent could also be applied to allow for the present system to work. It is also believed that the attitudes of fear and distrust would lead individuals to automatically removing themselves from the list of presumed donors. This system of presumed consent is practiced in several European countries with a notable increase in transplants per million people. Even with presumed consent the supply of organs still would not meet the current demand. Presently in the United States there are several states that have presumed consent legislation surrounding cornea procurement.

The idea of providing financial incentives for organ donation is a continued debate. Since the passage of the National Organ Transplant Act of 1984, federal law prohibits the buying and selling of organs in the United States. There have been many different proposals for using financial incentives to increase organ donation ranging from tax credits, payment for funeral expenses, direct monetary payments for donation itself or for signing a donor card. This also becomes more expanded into brokered donation for living donors of kidneys which is practiced in some third world countries. One of the main arguments against this practice is the possibility of exploiting the poor and minority groups. If such a system is implemented the

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exchange of donated organs to recipeints would turn into a market system. There would be living and or cadaveric donors who are considered vendors of commodities. This then opens to a varity of procedural issues; who would pay for the organs, who would be responsible for regulating this "market"—the government or the OPO, would there be a different fee for each organ recovered, what if consent was granted but the organs were unsuitable, etc. Where as the idea of a cash benefit may be offensive, the allowance towards funeral expenses is easier for some to consider. A recent national poll developed by the National Kidney Foundation and UNOS showed the traditional attitudes towards organ transplants are changing. In the poll, four groups (African-Americans, Hispanics, those with income under 20,000 a year, and those between the ages of 18 and 24) were in favor of presumed consent and financial compensation. With the gowing list of waiting recipients the idea of compensation and implied consent are no longer unthinkable but are receiving significant support in view of the critical shortage of available organs, This support is especially surprising in view of no public education on the issues and only limited public debate.

In attempts to increase the supply of cadaveric organs for transplants many centers are instituting protocols to recover kidneys from asystolic donors. There is also the increasing use of unrelated living ranal donation. Xenograft transplantation may also receive more focus in the future. But before any of these new ideas or a change in the current donation system can be implemented, more public debate, education and concensus must occur. ■

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Non-Linear Dynamics and Everything

The following was contributed by H.R. Plessman, Ph.D., who is the Markel Professor of Biology at the University of Salt Lake City.

Non-linear dynamics is a mathematical theory (also called "Chaos theory") which may be as revolutionary to science as any previous unifying theory (the cell theory, the theory of evolution, etc.) It is likely that the theory would not have been discovered without the invention of the personal computer; in fact, one of the first (trivial) applications of the theory are Mandelbrot equations, which, when programed into a computer, can generate enormously complex and ordered figures.

The challenge for the sciences will be to predict the patterns which emerge from simple interactions between the units making up a larger structure.

Chaos theory, in fact, deals with the interface between order and random events. The ultimate structure of a snowflake, for example, would be intrinsically predictable if the arrangement of the first few water atoms could be known; likewise, the ultimate size and shape of a tree could in theory be predicted by knowing the exact arrangement of molecules in the seed (and a few things about environmental influences, of course).

Chaos theory implies that if a number of particles can interact with each other, order will emerge. Another way of putting it is that the structure of any material thing depends on the interaction of its particular building blocks, and is not imposed from outside. There are several areas where chaos theory seems to explain things previously unexplained.

Astronomy;

The farther we have been able to peer into space, the stranger things seem to be. One previously unexplained observation has to do with the large scale order of the universe. When groupings of galactic clusters are observed, they do not distribute at random, but rather, in an orderly, almost crystalline pattern. This is in contradiction to previous theories, which held that on the large

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scale, the order of the universe should be random, since origination from a single "Big Bang" would predict random distribution. Chaos theory, of course, would predict that the gravitational interaction of component galaxies would intrinsically lead to an orderly distribution.

Consciousness:

The brain has been shown to function as a massive parallel computer. This implies that literally millions of interactions are taking place simultaneously and influencing each other. The "hard-wiring" of the brain is a function of neuronal interaction, and can be explained by non-linear dynamics. Of greater interest, however, is the observation that we are "conscious" of one event at a time, and when we think, we perform as a serial rather than a parallel computer.

From a neurobiologic standpoint, there is no point in the brain which acts as a symphony conductor, or a pilot, or homunculus. Instead, consciousness seems to be the ability to voluntarily create internal states (neurologic reactions) which would normally be created by external influences. In human development, these states are intitially associated with words. In studies it appears that human beings only become "conscious" after developing a certain competency in language; Helen Keller, who learned language in her early teens, was unable to recall anything prior to that point. The earliest memories of most people are of ages three or four, and this seems to be about when complex language finally becomes possible (as opposed to simple words and phrases). In some languages, competency develops later than in others, and earliest memories are proportional.

There have been experiments of nature in which there has been temporary global aphasia. Although the patient appears to be conscious in every way, memories of this period are extremely fragmentary after recovery of language.

Consciousness, then, is viewed as a pattern imposed upon the massive parallel computer by the neurobiologic changes achieved by a certain threshold number of words, which influence each other, and produce the pattern that seems to be "self-awareness".

Historical Evolution:

Why is it that the pyramids in Mexico and the pyramids in Egypt, and other massive structures built by man all date from more or less the same historical epoch? Why did primitive religion more or less die out, to be replaced by various monotheristic formulations, all within a very short span of history? Why did monarchies evolve from tribes and nations emerge from monarchies, almost as if programmed? These kinds of questions have led to many different theories, from Aristotle to Marx. However, from the standpoint of chaos theory, the interaction of increasing numbers of human beings in a given region would be expected to produce new and unexpected patterns. This of course gives pause to the idea that we can actually predict historical change and new human organizations unless we get a much better grip on chaos theory.

Organic Evolution:

While the theory of natural selection has tremendous impact on modern biology, it does not totally explain why over several millennia, the number of species grew at a very slow rate; then there was an enormous flowering of species over a relatively brief period of time; followed by another epoch (which we are still in) in which species are emerging at a very slow rate. The explanation for this seems to be provided by chaos theory as well. The number of different types of cells in an organism are related to the number of genes in the genome; humans have about 300, whereas primitive flatworms may have only ten or twelve. Its relatively easy to see that at some point in evolution, as the number of different genes reached a certain threshold, the patterns that were possible suddenly increased dramatically, even though the genetic complement had only increased slightly.

Human Biology:

The last decade was a vast unfolding of molecular biology, which continues today. As we continue to discover new cell-cell interactions, it seems as though we are on the threshold of solving the problems of aging, heart disease, cancer, etc. However, one of the puzzles of modern biology is that specific manipulation of cell interactions does not result in predictable outcomes on an organism level. This is especially apparent in cancer therapy, where treatments are designed to disturb the

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Non-Linear Dynamics

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genetic complement of the cancer cell; but paradoxically, cancers which survive tend to proliferate and invade even more aggressively, while becoming resistant. The origin of cancer itself is explainable as a disturbance in the pattern which exists because of the normal genome. Alterations in the genetic code caused by cancer treatment can in turn result in different quality interactions which result in further proliferation and invasion.

The simple interaction between cells, words, genes, galaxies, and so forth are readily described. The challenge for the sciences in the next century will be to develop a method for predicting the patterns resulting from these interactions, which is possible in theory. Once this is accomplished, not only will we have a powerful new tool for medicine, but also we should be able to predict economic and social changes on a broad scale with a striking degree of accuracy. At that point, social engineering becomes possible, for good or for bad. ■

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Baystate Medical Center 1984-1985 (Internal Medicine)
Residency: Health Center Hospital, Pennsylvania 1974-1976 (Pathology)
Baystate Medical Center 1985-1987 (Internal Medicine)
Specialty: Internal Medicine

Gino Mercadante, D.O.
222 Carew Street
Springfield, MA 01104

Born: July 2, 1959
Premed: Springfield College 1977-1981
Medical: University of New England College of Osteopathic Medicine 1983-1987
Internship: Metropolitan General Hospital, Florida 1987-1988
Residency: Berkshire Medical Center, Pittsfield, MA 1988-1991
Specialty: Internal Medicine

David P. Norton, M.D.
444 Montgomery Street
Chicopee, MA 01020

Born: June 15, 1956
Premed: Georgetown University 1975-1979
Medical: Yale University School of Medicine 1979-1983
Internship: University of California, San Francisco 1983-1984
Residency: University of California 1984-1986
Specialty: Pediatrics

Peggy M. Bissell, M.D.
Baystate Medical Center
759 Chestnut Street
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Born: September 24, 1950
Premed: Mount Holyoke College, MA 1968-1972
Northeastern University 1973-1976
Medical: University of Massachusetts Medical School 1978-1983
Internship: Worcester Memorial Hospital 1983-1984
Residency: Worcester Memorial Hospital 1984-1986
Specialty: Emergency Medicine

Paul M. Gagnon, D.O.
Providence Hospital
1233 Main Street
Holyoke, MA 01040

Born: June 22, 1960
Premed: University of Rhode Island 1979-1983
University of Massachusetts Sept. 1978-Dec. 1978
Medical: New England College of Osteopathic Medicine 1983-1987
Internship: Michigan Osteopathic Medical Center, MI 1987-1988
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Specialty: General Surgery

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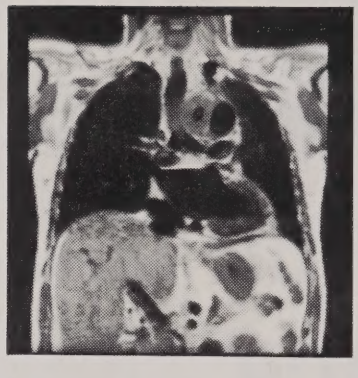

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